

**Listing of Claims:**

This listing of claims reflects all claim amendments and replaces all prior versions, and listings, of claims in the application (material to be inserted in amended claims is in **bold and underline**, and material to be deleted is in ~~[brackets and strikeout]~~).

1.-93. Canceled (without prejudice).

94. (Amended) A method of detecting the activity of an enzyme that operates on a substrate to form a product in a sample, comprising:

contacting the substrate with the enzyme **in the sample**; ~~to form~~

contacting the **sample** ~~[substrate or any product produced by operation of the enzyme]~~ with a binding partner that specifically binds to the **substrate** or to **a (the) product of the operation of the enzyme**, but not to both, wherein the binding partner includes gallium that is required for binding between the binding partner and the substrate or **the** product;

detecting a response, based on luminescence polarization, indicative of the extent of binding between the substrate or the product and the binding partner without separating the bound substrate or product from the unbound substrate or product; and

correlating the response with the activity of the enzyme.

95. (Original) The method of claim 94, wherein the step of detecting a response comprises:

exposing the sample to polarized light; and

measuring the degree of polarization of light emitted from the sample, in response to the step of exposing, wherein the degree of polarization is indicative of the extent of binding between the substrate or product and the binding partner.

3 96. (Original) The method of claim 95, further comprising determining the degree of polarization of the emitted light using a function selected from the group consisting of polarization and anisotropy.

97. (Original) The method of claim 94, wherein the substrate is a polypeptide, and wherein the substrate and product are related by a posttranslational modification.

98. (Original) The method of claim 97, wherein the posttranslational modification is phosphorylation or dephosphorylation of the polypeptide.

99. (Original) The method of claim 98, wherein the substrate and product are luminescent.

DI 100. (Original) The method of claim 99, wherein the enzyme is a kinase, wherein the posttranslational modification is phosphorylation of the substrate, wherein the binding partner specifically binds to the product but not to the substrate, and wherein the degree of polarization of light emitted from the sample is higher when the enzyme is operative to form the product from the substrate than when the enzyme is inoperative or absent.

101. (Original) The method of claim 99, wherein the enzyme is a phosphatase, wherein the posttranslational modification is dephosphorylation of the substrate, wherein the binding partner specifically binds to the substrate but not to the product, and wherein the degree of polarization of light emitted from the sample is lower when

the enzyme is operative to form the product from the substrate than when the enzyme is inoperative or absent.

102. (Original) The method of claim 94, wherein the substrate is a nucleotide, and wherein the substrate and product are related by a cyclization or decyclization of the nucleotide.

103. (Original) The method of claim 102, wherein the substrate and product are luminescent.

DI 104. (Original) The method of claim 103, wherein the enzyme is a phosphodiesterase, wherein the substrate is a cyclic nucleotide, wherein the product is a nucleotide monophosphate formed by decyclization of the substrate, wherein the binding partner specifically binds to the product but not to the substrate, and wherein the degree of polarization of light emitted from the sample is higher when the enzyme is operative to form the product from the substrate than when the enzyme is inoperative to absent.

105. (Original) The method of claim 103, wherein the enzyme is a cyclase, wherein the substrate is a nucleotide monophosphate, wherein the product is a cyclic nucleotide formed by cyclization of the substrate, wherein the binding partner specifically binds to the substrate but not to the product, and wherein the degree of polarization of light emitted from the sample is lower when the enzyme is operative to form the product from the substrate than when the enzyme is inoperative or absent.

106. Canceled (without prejudice).

107. Canceled (without prejudice).

108. (Original) The method of claim 94, wherein the enzyme is selected from the group consisting of kinases and phosphatases.

109. (Original) The method of claim 94, wherein the enzyme is selected from the group consisting of cyclases and phosphodiesterases.

110. (Original) The method of claim 94, wherein the substrate includes a phosphorylated polypeptide or a nonphosphorylated polypeptide.

111. (Original) The method of claim 94, wherein the substrate includes a cyclized nucleotide or a noncyclized nucleotide.

112. (Original) The method of claim 94, further comprising:  
contacting the substrate and enzyme with a candidate compound; and  
determining the ability of the candidate compound to enhance or inhibit enzyme activity by its effects on the response.

113. (Original) The method of claim 94, the binding between the binding partner and the substrate or product being characterized by a binding coefficient, wherein the binding coefficient is no larger than about  $10^{-8}$  M.

114. (Original) The method of claim 94, further comprising:  
providing a sample holder having a plurality of sample sites supporting a corresponding plurality of samples; and

repeating the steps of contacting, detecting, and correlating for each of the plurality of samples.

115. (Original) The method of claim 94, wherein the step of contacting the substrate with the enzyme precedes the step of contacting the substrate or any product produced by operation of the enzyme with a binding partner.